REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The November 27, 2007, personal interview between Examiners Liu, Schultz, and Epperson and applicants' undersigned attorney is gratefully acknowledged. The substance of that interview is summarized below.

It is recognized that 37 CFR § 1.111(a)(2) states that a reply that is a supplement to a reply that is in compliance with 37 CFR § 1.111(b) will not be entered as a matter of right. However, it is respectfully requested that the U.S. Patent and Trademark Office enter this amendment which is submitted as a follow-up to the personal interview. The above amendments are made pursuant to the suggestions made by the examiners at the personal interview and are submitted in an effort to put the case in a better form for allowance or appeal.

Claims 89-112 and 148-153 are pending. Claim 89 is amended, and claims 149-153 are new. Support for these amendments/new claims is found in the present application at page 38, line 20 to page 39, line 9, page 40, lines 1 to 6, page 41, lines 1 to 2, page 42, lines 13 to 16, page 45, lines 10 to 11, and page 48, lines 31 to 33.

The rejection of claims 89, 93, and 148 under 35 U.S.C. § 102(b) as anticipated by Lipshutz et al., *Biotechniques* 19(3):442-447 (1995) ("Lipshutz") is respectfully traversed.

Lipshutz relates to a method of light-directed chemical synthesis to create high-density arrays of oligonucleotide probes, which can be used for detection of hybridized targets. In particular, this reference discloses the synthesis of an array of oligonucleotides in which linker molecules with a photochemically removable protective group are attached to a solid substrate. Light is directed through a photolithographic mask to specific areas of the surface, activating those areas for chemical coupling. The first of a series of nucleosides is incubated with the array, and chemical coupling occurs at those sites that have been illuminated in the preceding step. Next, light is directed to a different region of the substrate through a new mask, and the chemical cycle is repeated. The process is repeated.

In contrast, claim 89 is directed to a method of forming arrays of oligonucleotides on a solid support comprising forming an array of a plurality of capture oligonucleotides on the solid support by a series of cycles, each of the cycles comprising: activating selected array positions for attachment of multimer nucleotides; selecting multimer

nucleotides with nucleotide sequences differing from each other by at least 2 nucleotides, wherein no two dimers in the multimers are complementary to each other and the multimers would not result in self-pairing or hairpin formulation; and attaching multimer nucleotides at the activated array positions. The multimer nucleotides are selected so that the capture oligonucleotides formed by attachment of a plurality of the multimer nucleotides at each activated array position have nucleotide sequences selected to hybridize with complementary oligonucleotide target sequences under uniform hybridization conditions across the array of oligonucleotides and so that each of the capture oligonucleotides have substantial sequence differences to prevent cross-reactivity. Likewise, the subject matter of dependent claims 90, 105, 111, 112, and 149-153 is not taught by this reference.

Lipshutz neither discloses nor suggests forming an array of a plurality of capture oligonucleotides on the solid support by a series of cycles, each of the cycles comprising activating selected array positions for attachment of multimer nucleotides, selecting multimer nucleotides with the claimed characteristics, and attaching multimer nucleotides at the activated array positions. Instead, Lipshutz teaches attaching single nucleosides to sites that have been illuminated in the preceding step. As amended the claims can no longer be properly construed to read on Lipshutz's synthesis of oligomers. Simply stated, repeatedly adding one nucleoside to an array at a time is not the same as repeatedly putting a multimer on the array.

A further distinction is that Lipshutz neither discloses nor suggests using multimer nucleotides which are selected so that the capture oligonucleotides formed by attachment of a plurality of the multimer nucleotides at each activated array position hybridize to complementary oligonucleotides under uniform hybridization conditions across the array of oligonucleotides and so that each of the capture oligonucleotides have substantial sequence differences to prevent cross-reactivity, as required by the claims of the present application. In contrast, Lipshutz identifies the generation of signal from GC-rich and AT-rich probes (which have different hybridization strengths) in the same experiment as an "important challenge" to be met for broad implementation of the disclosed method (see page 7 of 7, col. 1, lines 21-30). This is an important distinction between Lipshutz and the claimed invention. In particular, the probes in Lipshutz's array carry the burden of both detecting a target nucleic acid and generating a signal correlated to detection of the target. Designing a plurality of capture probes capable of detecting and signaling detection of a plurality of different nucleic acid targets at one time on a single array (i.e. under uniform hybridization

conditions) is a difficult task using Lipshutz's technology. Moreover, since Lipshutz's capture probes must be capable of accomplishing the diverse tasks of detection and signaling, its system is particularly susceptible to producing false signals. By contrast, detection and signaling of such detection can be readily and accurately achieved with the device produced by the method of the present invention, because the above characteristics of the capture probes.

Accordingly, the rejection based on Lipshutz is improper and should be withdrawn.

The rejection of claims 89 and 93 under 35 U..C. § 102(b) as anticipated by Fodor et al., *Nature* 364:555-556 (1993) ("Fodor II") is respectfully traversed.

Fodor II relates to the synthesis of biological arrays by attaching linkers modified with photochemically removable protecting groups to a solid substrate. Light is directed through a photolithographic mask to specific areas of the surface effecting localized photodeprotection. The first of a series of chemical building blocks (e.g., hydroxyl photoprotected deoxynucleosides) is incubated with the surface, and chemical coupling occurs at those sites which have been illuminated in the preceding step. Next, light is directed to a different region of the substrate through a new mask, and the chemical cycle is repeated.

Fodor II neither discloses nor suggests forming arrays of oligonucleotides on a solid support comprising forming an array of a plurality of capture oligonucleotides on the solid support by a series of cycles, each of the cycles comprising activating selected array positions for attachment of multimer nucleotides, selecting multimer nucleotides with the claimed characteristics, and attaching multimer nucleotides at the activated array positions. The multimer nucleotides are selected so that the plurality of capture oligonucleotides formed by attachment of a plurality of the multimer nucleotides at each activated array position hybridize with complementary oligonucleotide target sequences under uniform hybridization conditions across the array of oligonucleotides and so that each of the capture oligonucleotides have substantial sequence differences to prevent cross-reactivity, as required by the claims of the present application. Likewise, the subject matter of dependent claims 90, 105, 111, 112, and 149-153 is not taught by this reference. Accordingly, for substantially the reasons noted above, the rejection based on Fodor II is improper and should be withdrawn.

The rejection of claims 89-93, 96-97, 109, 111, and 148 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,700,637 to Southern et. al., is respectfully traversed.

Southern discloses an apparatus and a method for analyzing polynucleotide sequences as well as a method of generating oligonucleotide arrays. The oligonucleotides forming the array are only disclosed to be formed from conventional nucleotides. Thus, Southern suffers from the same deficiencies as Lipshutz and fails to teach forming an array of a plurality of capture oligonucleotides on the solid support by a series of cycles, each of the cycles comprising activating selected array positions for attachment of multimer nucleotides, selecting multimer nucleotides with the claimed characteristics, and attaching multimer nucleotides at the activated array positions. The multimer nucleotides are selected so that the plurality of capture oligonucleotides formed by attachment of a plurality of the multimer nucleotides at each activated array position have nucleotide sequences selected to hybridize with complementary oligonucleotide target sequences under uniform hybridization conditions across the array of oligonucleotides and so that each of the capture oligonucleotides have substantial sequence differences to prevent cross-reactivity, as claimed. Likewise, the subject matter of dependent claims 90, 105, 111, 112, and 149-153 is not taught by this reference. Accordingly, the rejection based on Southern should be withdrawn.

The rejection of claims 89, 91, 93, 96, 111, and 148 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,837,832 to Chee et. al., is respectfully traversed.

Chee teaches arrays of nucleic acid probes on biological chips. Chee fails to teach forming arrays of oligonucleotides on a solid support comprising forming an array of a plurality of capture oligonucleotides on the solid support by a series of cycles, each of the cycles comprising activating selected array positions for attachment of multimer nucleotides, selecting multimer nucleotides with the claimed characteristics, and attaching multimer nucleotides at the activated array positions. The multimer nucleotides are selected so that the plurality of capture oligonucleotides formed by attachment of a plurality of the multimer nucleotides at each activated array position have nucleotide sequences selected to hybridize with complementary oligonucleotide target sequences under uniform hybridization conditions across the array of oligonucleotides and so that each of the capture oligonucleotides have substantial sequence differences to prevent cross-reactivity, as claimed. Likewise, the subject matter of dependent claims 90, 105, 111, 112, and 149-153 is not taught by this reference.

Therefore, Chee is distinguishable from the claimed invention for substantially the same reasons noted above, and the rejection based on this rejection should be withdrawn.

The rejection of claims 89-97, 109, 111-112, and 148 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,510,270 to Fodor et al. ("Fodor I") is respectfully traversed.

Fodor I relates to a method for synthesizing and screening polymers on a solid substrate. The method includes providing a substrate which may include linker molecules on its surface. On the substrate or a distal end of the linker molecules, a functional group with a protective group is provided. The protective group may be removed upon exposure to radiation, electric fields, electric currents, or other activators to expose the functional group. Using photolithographic methods, the protective group is removed in first selected regions and the substrate is contacted with a first monomer which reacts with the functional group. Thereafter, second selected regions are deprotected and exposed to a second monomer which reacts with the exposed functional group. These steps are repeated until the substrate includes desired polymers of desired lengths. Monomers may include amino acids, nucleotides, pentoses, and hexoses.

Fodor I neither discloses nor suggests forming arrays of oligonucleotides on a solid support comprising forming an array of a plurality of capture oligonucleotides on the solid support by a series of cycles, each of the cycles comprising activating selected array positions for attachment of multimer nucleotides, selecting multimer nucleotides with the claimed characteristics, and attaching multimer nucleotides at the activated array positions. The multimer nucleotides are selected so that the plurality of capture oligonucleotides formed by attachment of a plurality of the multimer nucleotides at each activated array position have nucleotide sequences selected to hybridize with complementary oligonucleotide target sequences under uniform hybridization conditions across the array of oligonucleotides and so that each of the capture oligonucleotides have substantial sequence differences to prevent cross-reactivity, as required by the claims of the present application. Likewise, the subject matter of dependent claims 90, 105, 111, 112, and 149-153 is not taught by this reference. Therefore, Fodor I is distinguishable from the claimed invention for substantially the same reasons noted above, and the rejection based on this reference should be withdrawn.

The rejection of claims 89-94, 96-97, 109, 111-112, and 148 under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 5,527,681 to Holmes ("Holmes") is respectfully traversed.

Holmes relates to methods, devices, and compositions for synthesis and use of diverse molecular sequences on a substrate. In particular, this reference discloses the synthesis of an array of polymers in which individual monomers in a lead polymer are systematically substituted with monomers from one or more basic sets of monomers. On the substrate or a distal end of linker molecules, a functional group with a protective group is provided. The protective group may be removed upon exposure to a chemical reagent, radiation, electric fields, electric currents, or other activators to expose the functional group. Using photolithographic methods, the protective group is removed in first selected regions and the substrate is contacted with a first monomer which reacts with the functional group. Thereafter, second selected regions are deprotected and exposed to a second monomer which reacts with the exposed functional group. These steps are repeated until the substrate includes desired polymers of desired lengths. Monomers may include amino acids, nucleotides, pentoses, and hexoses. Holmes neither discloses nor suggests forming arrays of oligonucleotides on a solid support comprising forming an array of a plurality of capture oligonucleotides on the solid support by a series of cycles, each of the cycles comprising activating selected array positions for attachment of multimer nucleotides, selecting multimer nucleotides with the claimed characteristics, and attaching multimer nucleotides at the activated array positions. The multimer nucleotides are selected so that the plurality of capture oligonucleotides formed by attachment of a plurality of the multimer nucleotides at each activated array position have nucleotide sequences selected to hybridize with complementary oligonucleotide target sequences under uniform hybridization conditions across the array of oligonucleotides and so that each of the capture oligonucleotides have substantial sequence differences to prevent cross-reactivity, as required by the claims of the present application. Likewise, the subject matter of dependent claims 90, 105, 111, 112, and 149-153 is not taught by this reference. Therefore, Holmes is distinguishable from the claimed invention for substantially the same reasons noted above, and the rejection based on this reference should be withdrawn.

The rejection of claims 89-97, 109, 111, 112, and 148 under 35 U.S.C. § 112 (2nd para.) for indefiniteness is respectfully traversed in view of the above amendments and the November 8, 2007, Amendment.

In view of the all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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